

REMARKS

Applicants file this Amendment in response to the Office Action mailed October 15, 2007. The Office Action set an initial due date for response of January 15, 2008, and Applicants file this Amendment concurrently with a Request for Three-Month Extension of Time and associated fee.

In the Action, the Office considers and rejects all pending claims, 1-19. The present Amendment amends claims 1, 2, 5, 6, 7, 16, and 17, and cancels claims 3, 9, 15, and 18-19. Claims 1-2, 4-8, 10-14, and 16-17 are pending and under consideration. The amendment of the claims finds support in the original claims and in the specification as filed, e.g., at page 4, line 18 through page 5, line 7; page 7, lines 18-19; page 9, lines 2-14; page 10, lines 17-19; page 11, lines 3-19; Examples 1-11 at pages 13-16, especially page 16, line 25 to page 17, line 2; and original claims 3, 9 and 15.

Claim of Priority

Applicants note that in the previous Office Action dated March 16, 2007, the Examiner acknowledged the claim to priority, but indicated that only "some" certified copies of the priority documents have been received. In the response filed September 14, 2007, Applicants respectfully requested the Examiner to clarify which priority documents the Patent Office has not received. However, the Final Office Action dated October 15, 2007 did not contain said clarification. Therefore, Applicants again respectfully request the Examiner to clarify which priority documents the Patent Office has not received. Applicants submit that all required priority documents have been provided, and in the absence of future clarification from the

Office, will assume the Office's previous indication of "some" priority documents having been received, was an error.

Claim Rejections – 35 U.S.C. § 102(b)

The Office Action rejects claims 1-12 and 14-19 under 35 U.S.C. § 102(b) as allegedly anticipated by Scott et al. (WO 01/28524; hereinafter SCOTT). Furthermore, the Office Action states that Applicants' previous arguments concerning the rejection of the claims under 35 U.S.C. § 102(b) as allegedly anticipated by SCOTT are not persuasive, alleging that the relevance of Applicants' assertions is unclear. The Office Action further alleges that the claims, as previously amended, did not preclude the microspheres containing therapeutic proteins, a complexing agent including sulfated polysaccharides, and further coated by a fatty acid or lipid. The Office Action further alleges that since Applicants' claims allegedly state that the mixture of protein and sulfated polysaccharide is encapsulated with hydrophobic material, SCOTT anticipates the claimed invention.

Applicants respectfully disagree with the rejection, and submit that the claimed and disclosed subject matter is not anticipated by SCOTT for at least the reasons set forth in Applicants' response filed September 14, 2007. Furthermore, claim 1 recites "[a] sustained release solid formulation characterized by comprising protein drug, sulfated polysaccharide, and hydrophobic material selected from fatty acid, pamoic acid, monoacyl glycerols, sorbitan fatty acid esters, diacyl glycerols, triglycerides, phospholipids, sphingosines, sphingolipids, waxes, and salts or derivatives thereof, wherein the pH of a mixture of the protein and sulfated polysaccharide is lower than the isoelectric point of the protein, and the mixture of protein and sulfated polysaccharide is encapsulated within a matrix of the hydrophobic material." In

contrast, the microspheres taught in SCOTT comprise bivalent cations and water soluble polymer (see, e.g., page 58, claim 1).

With regard to the process of preparing a sustained release solid formulation, Applicants submit that claim 7 recites “[a] process to prepare a sustained release solid protein drug characterized by comprising preparing a mixture of proteins and sulfated polysaccharides, suspending the mixture obtained in a non-aqueous solution containing hydrophobic materials selected from fatty acid, pamoic acid, monoacyl glycerols, sorbitan fatty acid esters, diacyl glycerols, triglycerides, phospholipids, sphingosines, sphingolipids, waxes, and salts or derivatives thereof, and removing a solvent from the suspension to obtain a solid protein drug, wherein the pH of the mixture of proteins and sulfated polysaccharides is lower than the isoelectric point of the protein.” In contrast, SCOTT teaches a method for forming a microsphere comprising: (1) forming an aqueous mixtures containing: (a) a carrier protein; (b) a water soluble polymer; (c) a first complexing agent that is a polyanionic polysaccharide; and (d) a second complexing agent that is a divalent metal cation selected from the group consisting of calcium and magnesium; (2) allowing the microspheres to form in the aqueous mixture; and (3) stabilizing the microspheres, preferably by contacting the microspheres with a cross-linking agent and/or exposing the microspheres to an energy source, preferably heat, under conditions sufficient to stabilize the microspheres (see, e.g., SCOTT at claim 19, pages 59-60). Applicants submit that the presently disclosed and claimed invention is therefore distinct from that disclosed in SCOTT.

Finally, Applicants submit that the differences between the microspheres taught by SCOTT and Applicants’ claimed product, as well as differences in the methods of making the microspheres disclosed in SCOTT and the presently claimed and disclosed methods, indicate that

the products of SCOTT and those of the presently claimed and disclosed invention are constitutionally different. For example, SCOTT fails to teach a sustained release formulation comprising a protein drug and a sulfated polysaccharide wherein the pH of the mixture of protein and sulfated polysaccharide is lower than the isoelectric point of the protein. Due to such differences, for example, Applicants submit that the instantly claimed and disclosed process results in a higher yield than that of SCOTT.

For at least the foregoing reasons, Applicants submit that the claims are not anticipated by SCOTT and respectfully request withdrawal of this rejection.

Claim Rejections - 35 U.S.C. § 103(a)

The Office Action also rejects claims 1-19 under 35 U.S.C. § 103(a) as allegedly unpatentable over SCOTT. The Office alleges that Applicants' claims "do not preclude the microparticles of Scott" and therefore "that any method described within Scott would be capable of producing the composition as currently claimed by applicants" (see page 4, first paragraph, of the Office Action mailed October 15, 2007). The Office Action further alleges that since SCOTT allegedly describes that spray drying is routinely used to dry microparticles, it would have been obvious to the skilled artisan that spray drying could be used to dry the microparticles recited.

In response, Applicants submit that the claimed and disclosed invention is not unpatentable over SCOTT. For at least the reasons set forth above in response to the rejection of claims 1-12 and 14-19 under 35 U.S.C. § 102(b), SCOTT fails to anticipate or to suggest the claimed and disclosed invention. Additionally, Applicants submit that the instant invention has advantages over the disclosure of SCOTT. For example, the presently claimed and disclosed


invention prevents degradation or denaturation of the protein drug, and increases yield as discussed above. Furthermore, and despite the Office's assertions to the contrary, there is nothing in SCOTT that would have led to the choice of spray drying – or any other method – that would have led to the presently claimed invention. Moreover, Applicants submit that even if, *arguendo*, Applicants' claims did not preclude the microparticles of Scott, one cannot conclude, as the Office has, that "any method described within Scott would be capable of producing the composition as currently claimed by applicants." The Office's assertion is simply without support.

In view of the foregoing remarks, Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness, and respectfully request withdrawal of the rejection under 35 U.S.C. 103(a).

Conclusion

In view of the foregoing remarks and amendments, Applicants respectfully submit that the claims are in condition for allowance. If there should be any questions, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,
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